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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,369	02/23/2004	Min Wan	D 2003.784 US	8537

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PATENT DEPARTMENT
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EXAMINER	
AUDET, MAURY A	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/785,369	WAN ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6-9 and 11-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,6-9,11,12 and 19-21* is/are allowed.

6)☒ Claim(s) *3 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/3/07, 7/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response of 7/3/07 is acknowledged. However, the present action is once again, made NON-FINAL, since the substance of the 35 USC 103 rejection has changed, upon reconsideration, and the previous indication of allowable subject matter vacated, in part. Applicant's argument's have been considered and are deemed persuasive in part.

Backdrop Election/Restrictions

Applicant's election without traverse of the species Glycine-Glycine and 25 mM, in the reply filed 10/11/06, is acknowledged. The traversal is on the ground(s) that a serious burden would not apply to a search of all dipeptides in the present invention, and that all can be searched and examined without imposing a serious burden on the Examiner. This is not found persuasive because a search each species is necessarily a distinct search, which may contain art does not anticipate or render obvious other species. In that respect an initial search, retrieval, and application of art over more than one species does constitute an undue search burden. However, commensurate with species practice, all species will ultimately be searched and examined should the elected species and the other species be found free of the art.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3 and 13-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barri et al. (US 2003/0045004 A1).

As discussed previously, Barri et al. teach the use of monomeric amino acids (e.g. listing by example lysine, glycine, arginine) and other enzymatic or non-enzymatic inhibitors of carbamylation, to inhibit or delay carbamylation of proteins in a urea or cyanate containing solution (abstract, para's 12, 28, 39-40, and claims 7-9, 18-19).

[As to rejections of claim 12 above, it is noted that the compounds used in therein inherently possess a buffering capacity of about neutral, absent evidence to the contrary].

Barri et al. teach inhibiting and/or delaying carbamylation of peptides using compounds other than ethylene diamine like compound. However, Barri et al. does not expressly teach a process using the term "solubilizing" or "purifying" said peptide (claims 4-5); that the protein is to be ribonuclease or RNase A (claims 6-7); or that the carbamylation percent protection of about 100% after three weeks, a compound concentration within the broad range of 1-150mM, or cyanate in the solution at a concentration of about 5mM (claims 8-9, and 11).

Previously, it was indicated that Barri et al. also did not render obvious the use of any dipeptide to carry out the same, since Barri et al. was exclusively drawn to the use of mono amino acids, with no express teaching, suggestion, or reasonable motivation (that could be made based on the prior art currently of record) to advance the mono amino acids to dipeptides for the same purpose. As Barri et al's literature review indicates (para 9):

"Very few studies have been aimed at the prevention of carbamylation, and all have involved lens [eye] protein. [ ] There are no studies in which any amino acid has been used to prevent carbamylation of proteins or lipids."

This reasoning has been vacated, in view of Barri et al. and the level of skill in the art by the ordinary peptide chemist working in this field at the time of the invention. Namely, one of skill in the art, based on the understanding of amino acid function and known side chain and termini interactions of amino acids, would have understood that if a single amino acid can carry out the above, then so too could any general dipeptide (two amino acids conjugated), tripeptide, tetrapeptide, decapeptide, etc. However, the selection of certain specific compounds from the latter, especially by a showing of unexpected results thereto, as Applicant has shown in those recited in claims 1, 6-9, 11-12 and new claims 19-21, would not necessarily have been obvious, absent more.

Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to use randomly use any mono amino acid or dipeptide (two amino acids) to inhibit or delay carbamylation of proteins in a urea or cyanate containing solution in Barri et al., because Barri et al. advantageously teach the use of any mono amino acid to carry out the same, of which two mono amino acids conjugated together (or three, or four, or 100) would carry out the same function of binding urea/cyanate to curb the binding to the active agent, absent evidence to the contrary of some unexpected results/better properties by one or more (as shown by Applicant s to certain of these compounds noted in claims 1, 6-9, 11-12 and new claims 19-21). The selection

of any dipeptide randomly to carry out that of a mono amino acid would have been merely a matter of routine optimization by one of ordinary skill in the art.

It would have been obvious to one of ordinary skill in the art at the time of the invention to "solubilize" or "purify" the peptides being inhibited or delayed from carbamylation in any of the references above, because these "terms of art" are merely known objectives (solubilizing/purifying) to one of skill in the art in general peptide preparation, and more specifically are the desired end result beneficially taught by references, by using the underlying intermediate step of inhibiting or delaying carbamylation of peptides.

It would have been obvious to one of ordinary skill in the art at the time of the invention to apply inhibiting or delaying carbamylation to the specific peptide/protein of ribonuclease/RNase A in any of the references above, because these are merely well known peptides in the art which the references' teachings were expected to be applied, like the peptides of example the references beneficially taught the inhibition or delaying of carbamylation therein.

If not inherently in the references, it would have been obvious to one of ordinary skill in the art at the time of the invention to arrive at a carbamylation percent protection of about 100% after three weeks, a compound concentration within the broad range of 1-150mM, and cyanate in the solution at a concentration of about 5mM, in the references above, because the references all advantageously teach the use of like compounds to carry out the decarbamylation of peptides (the underlying process), and arriving at the above ranges to carry out the same process is merely

a matter of routine optimization by one of ordinary skill in the art, depending on the desired effect.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Allowable Subject Matter

Claims 1, 6-9, 11-12 and new claims 19-21, as drawn to a method for inhibiting and/or delaying carbamylation of a peptide in a urea or cyanate solution, using the specific compounds tested, namely glycinamide, histidine, 4-hydroxyl praline, Gly-Gly, and Gly-His, were not reasonably taught or suggested by the prior art of record. Namely, Barri et al. is the closest prior art, but is not drawn to the use of nay of these compounds.

Conclusion

Claims 1, 6-9, 11-12 and 19-21 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 12/22/06

CHRISTOPHER R. TATE
PRIMARY EXAMINER